REMARKS

Claims 1-20 were originally filed. Claims 1-14 were elected as Group I in the reply filed on 18 August 2004. Claims 15-20 are cancelled as unelected claims subject to the Restriction Requirement of 22 June 2004. Claims 21-24 were submitted as new in the Amendment of 19 January 2005 but these claims were not entered and withdrawn from consideration in the Office Action of 7 April 2005.

By this amendment, claims 1-24 are cancelled. Claims 25-34 are presented as new. Claims 25-34 are believed consonant with Group I of the Restriction Requirement as drawn to a method for identifying compounds that bind to a target of interest. Following entry of this amendment, claims 25-34 will be pending. No new matter is added by the amendments.

Rejection under 35 USC § 112, second paragraph

Claims 1-14 stand rejected under 35 USC § 112, second paragraph as allegedly indefinite. Claim 1 is allegedly vague and indefinite because the preamble does not correlate with the body of the claim, it is unclear if the two members are linked together while bound to the target, and the recitations of the terms "member", "members", and "target binding ligands" are unclear.

The rejection is rendered moot by cancellation of claims 1-14. Furthermore, new independent claim 25 is believed to be clear and definite. In the method of claim 25, members of a first and second set of ligands which bind to a target biomolecule are selected and then chemically linked to form a compound. The members have the property of binding to binding sites of a target. The compound is contacted with the target and the binding of the compound and the target is detected by mass spectrometry. Thus the preamble correlates with the body of the claim in identifying compounds that bind to a target of interest.

Claim 25 is not limited to linking the members while bound to target. In fact, Example 4 (pages 47-49 application as filed, and [0147-0149] US 2002/0172967 as published) shows a variety of compounds formed by linking an acetohydroxamic acid member to a phenylacetamide member by a solid phase coupling reaction, not in the

presence of target. Then, the binding affinity of the compounds, i.e. linked ligands, to stromelysin was tested, and ranged from 93 μ M to 350 μ M.

Rejection under 35 USC § 102(b)

Claims 1 and 6-12 stand rejected under 35 USC § 102(b) as allegedly anticipated by Shuker et al (1996) "Discovering High-Affinity Ligands for Proteins: SAR by NMR", Science, Vol. 274, 1531-1534, ("Shuker").

The rejection is rendered moot by cancellation of claims 1-14. Furthermore, Shuker does not disclose mass spectrometry as a means to detect binding a compound or a ligand to a target. Shuker discloses the unrelated analytic technique, nuclear magnetic resonance (NMR). Shuker teaches obtaining structure-activity relationships (SAR) of compounds or ligands (small organic molecules) in binding to proteins. SAR in Shuker is established by measuring changes in the NMR spectra of the target protein. Shuker does not directly detect, by any means, compounds or ligands which bind to target. In the present invention, the non-covalent binding of the compound to the target is detected by mass spectrometry. Therefore, Shuker does not anticipate the presently pending claims of the present invention.

Rejection under 35 USC § 103(a)

Claim 2-4 stand rejected under 35 USC § 103(a) as allegedly unpatentable over Shuker in view of Crooke et al US 2002/102572, ("Crooke").

The rejection is rendered moot by cancellation of claims 2-4. Furthermore, Shuker does not disclose or suggest mass spectrometry detection of non-covalent binding of a compound to a target. As the Examiner acknowledges, "Shuker et al differ from the instant invention in failing to teach the assembling step of (a) or (b) comprises measuring non-covalent binding of target binding ligands to the target by mass spectroscopy."

The Examiner alleges that "Crooke et al discloses that the mass spectrometry provides for advances over known techniques such as NMR." The applicant is unable to find any such disclosure in Crooke. In fact, a seemingly exhaustive recitation of other approaches to screening by Crooke [0004] includes sequencing of proteins and nucleic acids, NMR, X-ray crystallography, computer algorithms, ELISA, surface-plasmon resonance, and scintillation proximity assays, but does not include mass spectrometry.

Crooke does not disclose or suggest selecting two or more ligands which bind to different or the same binding sites of a target and chemically linking them together. Since Shuker does not disclose or suggest mass spectrometry detection of non-covalent binding of a compound to a target, the motivation to combine these references to make obvious the claims of the present invention is lacking.

Claim 5 stands rejected under 35 USC § 103(a) as allegedly unpatentable over Shuker in view of Wells et al WO 00/00823, ("Wells").

The rejection is rendered moot by cancellation of claim 5. Furthermore, Wells does not disclose or suggest detecting by mass spectrometry the non-covalent binding of a compound to a target where the compound is formed by chemically linking two ligands which bind to the target. Since Shuker does not disclose or suggest mass spectrometry detection of non-covalent binding of a compound to a target, the motivation to combine these references to make obvious the claims of the present invention is lacking.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation to combine the prior art references. There must also be a reasonable expectation of success in combining the references to practice the claimed invention. For the reasons cited above, the requisite suggestion, motivation, and expectation of success has not been demonstrated to render the present claims of the invention obvious.

Conclusion

With respect to any and all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter, and moreover have not acquiesced to any objection and/or rejection made by the Office. Applicants expressly reserve the right to pursue prosecution of any subject matter not presently claimed in one or more future or pending continuation and/or divisional applications.

In view of the above, reconsideration and allowance of this application are now believed to be in order. Applicants respectfully request that a timely Notice of Allowance be issued in this case. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at the number indicated below.

Respectfully submitted, GENENTECH, INC.

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